INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/07748

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) : C12Q 1/68; C07H 21/04
US CL : 435/6; 536/23.1, 23.5
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/6; 536/23.1, 23.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,776,683 A (SMITH et al) 07 July 1998 (07.07.1998), especially col. 6, 25 and Table 7.	1-4
Y	SQUIRE et al. High-resolution mapping of amplifications and deletions in pediatric osteosarcoma by use of CGH analysis of cDNA microarrays. Genes, Chromosomes & Cancer. 2003, Vol. 38, pages 215-225, especially page 216 and Table 1.	1-4

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
18 January 2006 (18.01.2006)

Date of mailing of the international search report
21 FEB 2006

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Form PCT/ISA/210 (second sheet) (April 2005)

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-4, with respect to the amplicon comprising chromosome 8q24.13

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐

INTERNATIONAL SEARCH REPORT

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BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional examination fees must be paid.

Groups 1-47, claims 1-4 (in part), drawn to methods for identifying an antineoplastic agent by contacting a test compound with a cell containing one of the 47 amplicons set forth in Table 2. For example, Group 1 is drawn to methods for identifying an antineoplastic agent by contacting a test compound with a cell containing the 5.3 MB amplicon comprising chromosome 8q24.13. Upon election of one of the groups, please specify the amplicon to be searched.

Groups 48-3097, claims 5-9 (in part), drawn to methods for identifying an antineoplastic agent by contacting a test compound with a cell containing one of the sequences of SEQ ID NO: 1-3049 and assaying for a change in the level of expression of one of the sequences. For example, Group 48 is drawn to methods for identifying an antineoplastic agent by contacting a test compound with a cell containing SEQ ID NO: 1. Upon election of one of the groups, please specify the SEQ ID NO of the elected group to be searched.

Groups 3098-6147, claims 10-11 (in part), drawn to methods for identifying a cancerous state of a cell by assaying for the sequence of one of SEQ ID NO: 1-3049. Upon election of one of the groups, please specify the SEQ ID NO of the elected group to be searched.

Groups 6148-9196, claims 12-34 (in part), drawn to methods for identifying an antineoplastic agent by contacting a test compound with a cell containing a polypeptide encoded by one of the sequences of SEQ ID NO: 1-3049 and assaying for a change in the activity of the polypeptide. Upon election of one of the groups, please specify the SEQ ID NO of the elected group to be searched. Further, it is noted that claim 23 has been included with this grouping because it appears that claim 23 intends to depend from claim 15, rather than claim 11.

Groups 9197-12,245, claims 35-39 (in part), drawn to methods for identifying an antineoplastic agent by contacting a test compound with a cell containing one of the sequences of SEQ ID NO: 1-3049 and assaying for a change in the cancer cell growth of said cell. Upon election of one of the groups, please specify the SEQ ID NO of the elected group to be searched.

Groups 12,246-15,294, claims 40-47 (in part), drawn to methods for treating cancer by using a compound that effects the activity of a polypeptide encoded by one of the sequences of SEQ ID NO: 1-3049. Upon election of one of the groups, please specify the corresponding SEQ ID NO of the elected group to be searched.

Groups 15295-18343, claims 48-55 and 57-60 (in part), drawn to methods for monitoring the progress of a cancer therapy by assaying for the level of a polypeptide encoded by one of the sequences of SEQ ID NO: 1-3049. Upon election of one of the groups, please specify the SEQ ID NO of the elected group to be searched.

Groups 18,344-21,392, claim 56 (in part), drawn to methods for producing data comprising producing test data sufficient to identify the chemical nature of a test compound that effects the activity of a polypeptide encoded by one of the sequences of SEQ ID NO: 1-3049. Upon election of one of the groups, please specify the SEQ ID NO of the elected group to be searched.

The inventions listed as Groups 1-21,392 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

In accordance with 37 CFR 1.475(d) Applicant is entitled to an examination of the first product, method of making said product and method of using said product. In the instant case, the first method is one which requires one of the 47 amplicons of Table 2. This product is not required for the methods set forth in the remaining groups. Thereby, Groups 48-21,392 constitute distinct groups which do not share the same corresponding technical feature of groups 1-47. Further, unity of invention exists only when there is a technical relationship among those inventions involving one or more of the same or corresponding technical features. The expression 'special technical feature" means those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. The technical feature linking the claims 5-60 is the HAS2 gene. However, the HAS2 gene was known in the art at the time the invention was and thereby does not constitute a contribution over the prior art (see NCBI Database, GenBank Accession No. U54804). Accordingly, there is no special technical feature linking the recited groups, as would be necessary to fulfill the requirement for unity of invention.

It is also noted that each of the present claims has been presented in improper Markush format, as distinct methods are improperly joined in the claims. Each amplicon of Table 2 and each nucleic acid sequence of SEQ ID NO: 1-3049 is structurally and functionally distinct from and has a different special technical feature than each other the amplicons and nucleic acid sequences. The chemical structure of each amplicon and nucleic acid sequence differ from each other. For example, a polynucleotide comprising SEQ ID NO: 1 is chemically, structurally, and functionally different from a molecule comprising SEQ ID NO: 2. Given the differences in the structure, function and effect the amplicons of Table 2 and the sequences of SEQ ID NO: 1-3049, these compounds are not considered to share a special technical feature as would be necessary to fulfill the requirement for unity of invention. These distinct compounds do not have both a "common property or activity" and a common structure as would be required to show that the inventions are "of a similar nature." As the products and methods encompassed by the claims do not share a special technical feature, the distinct products and methods may not properly be presented in the alternative. Accordingly, the claims have been separated into a number of groups corresponding to the number of different inventions encompassed by the claims, and the claims will be searched only as they read upon the invention of the elected group

Additionally, each of the claimed methods have different objectives and require different process steps. The methods of claims 1-4 require cells containing one of the amplicons of Table 2 and requires assaying for a change in the amplification ratio of the amplicon. The methods of claims 5-9 require the use cells that contain one of the sequences of SEQ ID NO: 1-3049, and requires assaying for a change in gene expression by assaying for mRNA or protein levels in order to accomplish the objective of identifying a antineoplastic agent. The methods of claims 10-11 require assaying for the level of one of the sequences of SEQ ID NO: 1-3049 in order to accomplish the objective of identifying a cancerous state of a cell. The methods of claims 12-34 require contacting a cell with a test agent and assaying for a change in biological activity of a polypeptide encoded by SEQ ID NO: 1-3049. The methods of claims 35-39 require contacting a cell with a test compound and assaying for the cancerous state of a cell. The methods of claims 40-47 require administering an agent to an individual in order to accomplish the objective of treating cancer. The methods of claims 48-55 and 57-60 require determining gene expression levels of a polypeptide of one of SEQ ID NO: 1-3049 and assaying for polypeptide levels in order to accomplish the objective of monitoring the progress of cancer therapy. The method of claim 56 requires identifying test compounds that have

antineoplastic activity and producing test data in order to obtain sufficient data to identify the chemical structure of the test compound. In addition to differences in objectives, effects, and method steps, it is again noted that the claims of the present Groups are not directed to the detection or identification of molecules having the same or common special technical feature, for the reasons discussed above.

Continuation of B. FIELDS SEARCHED Item 3:
WEST: USPT, JPAB, EPAB, DWPI, PGPUB; DIALOG: MEDLINE, CA, BIOSIS, EMBASE
search terms: 8q24.13, 8q24.1; amplification or amplified or copy number; cancer or tumor or neoplasm